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PATENT & TRADEMARK OFFICE
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AMENDMENT

IN THE CLAIMS:

Please cancel Claim 38 without prejudice.

Please amend the claims as follows:

1. (Amended) A [chimerical] chimeric peptide-nucleic acid fragment capable of entering a cellular compartment, comprising:

(a) a [cell-specific,] compartment-specific [or membrane-specific] signal peptide[, with the exception of a KDEL signal sequence,];

(b) a linkage agent[,]; and

(c) a nucleic acid [(oligonucleotide),] which is capable of entering a cellular pore;

wherein [the signal peptide being linked via] the linkage agent links [which via] an amino acid[s] at the carboxy-terminal end of the signal peptide [is linked therewith so as to ensure the appropriate nucleic acid introduction into cell organelles and cells] to the nucleic acid and wherein the signal peptide is specific to a compartment selected from the group consisting of mitochondria and chloroplasts.

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2. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the nucleic acid [consists of] comprises at least two bases.

3. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 2, wherein the nucleic acid [has] comprises a secondary structure.

4. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 2, wherein the sequence of the nucleic acid [has a] is partially palindromic [sequence].

5. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 4, wherein the nucleic acid may form a ["]hairpin loop["].

6. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 5, wherein the nucleic acid [may hybridize with] hybridizes to itself and [may] form a linear single-strand structure with an overhanging 3' end[or 5' end ('sticky end')].

7. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the nucleic acid is selected from the group consisting of [a] ribonucleic acid[, preferably a] and deoxyribonucleic acid.

8. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 7, wherein the phosphorous diester bonds of the nucleic acid [has chemically modified] are substituted with [']phosphorus thioate['] [linkages] bonds.

9. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the nucleic acid carries a reactive linkage group.

10. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 9, wherein the reactive linkage group contains an amino function [when] and the linkage agent contains an amino-reactive [grouping] group.

11. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 9, wherein the reactive linkage group contains a thiol function [when] and the linkage agent contains a thiol-reactive [grouping] group.

12. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 10 or 11, wherein the linkage [grouping] group present is bound to the nucleic acid via at least one C2 spacer[, but preferably one C6 spacer].

13. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 12, wherein the linkage [grouping] group is localized at [the] a position selected from the group consisting of the 3' hydroxy/phosphate terminus of the nucleic acid and [or at] the 5' hydroxy/phosphate terminus of the nucleic acid[, but preferably at the base].

14. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 12, wherein [defined] the nucleic acid[s,] is selected from the group consisting of [antisense oligonucleotides,] messenger RNAs, [or] transcribable genes and[/or] replicatable genes and wherein said nucleic acid is [are] linked at a position selected from the group consisting of [with] the 5' end and[/or] the 3' end.

15. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 14, wherein the nucleic acid to be linked [contains chemically modified] comprises [']phosphorus thioate['] [linkages] bonds.

16. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 14, wherein the gene to be linked contains a [promotor] promoter[, preferably a mitochondrial promoter].

17. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the signal peptide [has] comprises a reactive amino acid at the carboxy-terminal end, [preferably a lysine or cysteine, when] and the linkage agent contains an amino-reactive or thiol-reactive [grouping] group.

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18. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the signal peptide carries a [cell-specific,] compartment-specific [or membrane-specific] recognition [signal] sequence specific to a compartment selected from the group consisting of mitochondria and chloroplasts.

19. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the signal peptide [has] comprises a [cell-specific, compartment-specific or membrane-specific] peptidase cleavage site specific to a compartment selected from the group consisting of mitochondria and chloroplasts.

20. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the peptide [consists of] comprises the compartment-specific cleavable

signal peptide of the human mitochondrial ornithine transcarbamylase, extended by an [artificial] additional cysteine at the C terminus.

21. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to [any one of] claim 1, wherein the linkage agent is a bifunctional[, preferably heterobifunctional] cross-linker.

22. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the linkage agent [contains thiol-reactive and/or amino-reactive groupings when] and at least one of the signal peptide and the nucleic acid each carry a functional group selected from the group consisting of thiol-reactive and[/or] amino-reactive groups as linkage sites.

23. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the linkage agent is m-maleimido-benzoyl-N-hydroxy-succinimide ester or a derivative thereof.

24. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 1, wherein the molecule [can overcome] overcomes membranes with and without membrane potential by utilizing natural transport mechanisms.

25. (Twice amended) A [chimerical] chimeric peptide-nucleic acid fragment in the form of a linear-cyclic [plasmid] molecule, wherein the [plasmid] molecule comprises at least one replication origin and [that] both ends of the nucleic acid portion are cyclized, and wherein at least one cyclic end [having] comprises a modified nucleotide which via a linkage agent can be [liked] linked with a [cell-specific, compartment-specific or membrane-specific] signal peptide specific to a compartment selected from the group consisting of mitochondria and chloroplasts.

26. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid portion further comprises at least one promoter[,

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preferably a mitochondrial promoter, especially preferably the mitochondrial promoter of the light strand].

27. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid portion further comprises transcription-[regulatory] regulation sequences[, preferably mitochondrial transcription-regulatory sequences].

28. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the transcription-[regulatory] regulation sequences [have] comprise at least one binding site of a transcription initiation factor.

29. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to Claim 25, wherein the transcription-[regulatory] regulation sequences [have] comprise at least one binding site for [the] RNA synthesis apparatus[, preferably the binding site for the mitochondrial transcription factor 1 and the mitochondrial RNA polymerase].

30. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the transcription-[regulatory] regulation sequences are arranged [in] on the 3' [direction] side of the promoter.

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31. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [transcription is regulated by elements of the mitochondrial H-strand and L-strand] plasmid comprises transcription control elements which are suitable for H-strand and L-strand transcription of a mitochondrial genome.

32. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 31, wherein the ['conserved-sequence-blocks' of L-strand transcription act as] transcription control elements suitable for L-strand transcription are conserved-sequence-blocks.

33. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [plasmid] molecule further comprises at least one transcription termination site.

34. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the transcription termination site [has] comprises a binding sequence of a mitochondrial transcription termination factor.

35. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 34, wherein the [transcription termination site has the] binding sequence of [a preferably bidirectionally acting] the mitochondrial transcription termination factor is bidirectionally acting.

36. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the replication origin is a mitochondrial replication origin[, preferably the replication origin of the heavy mtDNA strand having at least one `conserved sequence block'].

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37. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [plasmid] molecule further comprises at least one [regulatory] regulation sequence for [the] replication.

39. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [plasmid] molecule further comprises a selection gene[, preferably an antibiotic-resistance gene, preferably the oligomycin - or chloramphenicol - resistance gene].

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40. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [plasmid] molecule further contains a multiple cloning site which permits the expression of [`]foreign genes[']].

41. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim [25] 40, wherein the multiple cloning site comprises recognition sequences for restriction endonucleases [which do preferably not occur in another site of the plasmid].

42. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the multiple cloning site is arranged in the 3' direction of the promoter and [in] on the 5' [direction] side of the transcription termination site.

43. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the multiple cloning site is arranged [in] on the 5' [direction] side of the selection gene.

44. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25 wherein the ends of the nucleic acid fragment [has (phosphorylated) ends] are [capable of litigation] joined to the peptide fragment by ligation.

45. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid fragment prior to cyclisation comprises a blunt end. [has `blunt ends' or overhanging 3' ends, preferably overhanging 5' ends.]

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46. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid fragment [has] prior to cyclisation comprises a 5' overhang which comprises 4 nucleotides [comprising 5' overhangs] with the proviso that the 4 nucleotides [which] do not have a self-homology [(palindromic sequence)] and are not complementary to one another [either].

47. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the ends of the nucleic acid fragment are cyclized via synthetic oligonucleotides.

48. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the overhanging 5' ends of the two oligonucleotides are complementary to one differing end of the nucleic acid each.

49. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein two differing [`]hairpin loops['] are used for the cyclization, one being specific (complementary) to the [`]left['] plasmid end and the other being specific to the [`]right['] plasmid end of the nucleic acid.

50. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the modified nucleotide is localized [preferably] within the [`loop'] cyclic portion.

51. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 25, wherein the [plasmid] molecule DNA is amplified enzymatically by suitable oligonucleotides which [have] comprise at least one recognition sequence for a restriction endonuclease [which occurs preferably in non-repeated fashion in the plasmid sequence].

52. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 51, wherein the restriction endonuclease to be used [generated] comprises an overhanging [ends,] end. [preferably 5' overhanging ends, the cleavage site being localized preferably outside the recognition sequence.]

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53. (Twice amended) The [chimerical] chimeric peptide-nucleic acid fragment according to claim 51, wherein the restriction endonuclease is B*sa*I.

54. (Twice amended) A process for the production of a [chimerical] chimeric peptide-nucleic acid fragment according to claim 1 or 25, comprising the following [stages] steps:

(a) reaction of a nucleic acid (oligonucleotide) containing a functional linkage group [having] which comprises a linkage agent[,];

(b) reaction of the construct of step (a) with amino acids at the carboxy-terminal end of a peptide, containing a signal sequence, with the exception of a KDEL signal sequence[,]; and

(c) [optionally] optional extension of the [chimerical] chimeric peptide-nucleic acid fragment of (b) by a further fragment selected from the group consisting of DNA or RNA [fragments].

55. (Twice amended) The process according to claim 54, wherein the DNA in step (c) is a PCR-amplified DNA fragment containing the human mitochondrial promoter of the light strand (P_L) as well as the gene for the mitochondrial transfer RNA leucine ($tRNALeu^{UUR)}$).

56. (Twice amended) [The] A process for the production of a [chimerical] chimeric peptide-nucleic acid fragment according to claim 1 or 25, comprising the following steps:

[(a) optional extension of the nucleic acid containing a functional linkage group by further DNA or RNA fragments,]

[(b)] (a) reaction of [the] a nucleic acid with a functional linkage group [or the extended nucleic acid of (a)] with a linkage agent,

[(c)] (b) reaction of the construct of [(b)] (a) with amino acids at the carboxy-terminal end of a peptide containing a signal sequence, with the exception of a KDEL signal sequence.

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57. (Twice amended) The process according to claim [56] 81, wherein the DNA fragment in step [(a)] (i) is a PCR-amplified DNA fragment containing the human mitochondrial promoter of the light strand (P_L) as well as the gene for the mitochondrial transfer RNA leucine ($tRNALeu^{UUR)}$).

58. (Twice amended) A method [to use] of using the [chimerical] chimeric peptide-nucleic acid fragment [according to] of claim 1 or 25 for introducing the [appropriate] nucleic

acid [introduction] into [cell organelles and] cells and mitochondria, comprising the step of reacting the fragment with cells or pretreated [cell compartments] mitochondria.

59. (Twice amended) The method [according to] of claim 58, wherein the pretreated cell compartments are energized mitochondria.

60. (Twice amended) A method of introducing [using] the [chimerical] chimeric peptide-nucleic acid fragment according to claims 1 or 25 [for the introduction] into eukaryotic cells.

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61. (Twice amended) The method according to claim 60, comprising [employing] the [`]particle gun['] system, electroporation, microinjection or lipotransfection for [the introduction] introducing the chimeric peptide-nucleic acid fragment into eukaryotic cells.

Please add new claims:

62. (New) The chimeric peptide-nucleic acid fragment according to claim 44 wherein the ends of the nucleic acid fragment are phosphorylated.

63. (New) The chimeric peptide-nucleic acid fragment according to claim 16, wherein the promoter is a mitochondrial promoter.

64. (New) The chimeric peptide-nucleic acid fragment according to claim 17, wherein the reactive amino acid at the carboxy-terminal end is a lysine or cysteine.

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65. (New) The chimeric peptide-nucleic acid fragment according to claim 21, wherein the linkage agent is a heterobifunctional cross-linker.

66. (New) The chimeric peptide-nucleic acid fragment according to claim 26, wherein the promoter is a mitochondrial promoter.

67. (New) The chimeric peptide-nucleic acid fragment according to claim 26, wherein the promoter is a mitochondrial promoter of the light strand.

68. (New) The chimeric peptide-nucleic acid fragment according to claim 27, wherein the transcription-regulatory sequences are mitochondrial transcription-regulatory sequences.

69. (New) The chimeric peptide-nucleic acid fragment according to Claim 29, wherein the binding site for the RNA synthesis apparatus comprises a binding site for the mitochondrial transcription factor 1 and a binding site for the mitochondrial RNA polymerase.

70. (New) The chimeric peptide-nucleic acid fragment according to claim 36, wherein the mitochondrial replication origin is the replication origin of the heavy mtDNA strand and comprises at least one conserved sequence block.

71. (New) The chimeric peptide-nucleic acid fragment according to claim 39, wherein the selection gene is an antibiotic-resistance gene.

72. (New) The chimeric peptide-nucleic acid fragment according to claim 39, wherein the selection gene is the oligomycin-resistance or chloramphenicol-resistance gene.

73. (New) The chimeric peptide-nucleic acid fragment according to claim 52, wherein the restriction endonuclease to be used comprises a 5' overhanging end.

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74. (New) The chimeric peptide-nucleic acid fragment according to claim 52, wherein the restriction endonuclease to be used comprises a cleavage site localized preferably outside the recognition sequence.

75. (New) The chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid fragment prior to cyclisation comprises an overhanging 3' end.

76. (New) The chimeric peptide-nucleic acid fragment according to claim 25, wherein the nucleic acid fragment prior to cyclisation comprises an overhanging 5' end.

77. (New) The chimeric peptide-nucleic acid fragment according to claim 51, wherein the recognition sequence for a restriction endonuclease occurs in non-repeated fashion in the molecule sequence.

78. (New) The chimeric peptide-nucleic acid fragment according to claim 10 or 11, wherein the linkage group present is bound to the nucleic acid via a C6 spacer.

79. (New) The chimeric peptide-nucleic acid fragment according to claim 12, wherein the linkage group is localized at the position of a modified nucleoside base on the nucleic acid.

80. (New) The chimeric peptide-nucleic acid fragment according to claim 40, wherein the recognition sequences for restriction endonucleases of which the multiple cloning site is comprised do not occur in another site of the molecule.

81. (New) A process for producing a chimeric peptide-nucleic acid fragment according to claim 1 or 25, comprising the steps:

(i) extension of a nucleic acid containing a functional linkage group by a fragment selected from the group consisting of DNA and RNA;

(ii) reaction of the fragment of step (i) with a linkage agent; and

(iii) reaction of the construct of (ii) with amino acids at the carboxy-terminal end of a peptide containing a signal sequence, with the exception of a KDEL signal sequence.

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82. (New) A method of introducing a nucleic acid with a functional linkage group into a compartment of a cell, comprising the steps:

(a) reaction of the nucleic acid with a linkage agent;

(b) reaction of the construct of step (a) with amino acids at the carboxy-terminal end of a peptide containing a signal sequence, with the exception of a KDEL signal sequence, to form a chimeric peptide-nucleic acid fragment; and

(c) contacting the chimeric peptide-nucleic acid fragment of step (b) with the cell;

wherein the signal sequence of the peptide is specific to a cell compartment selected from the group consisting of mitochondria and chloroplasts.